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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/058,546	04/10/1998	WALTER H. GUNZBURG	2316.1008-000	7592

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Interview Summary	Application No.	Applicant(s)	
	09/058,546	GUNZBURG ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Michael C. Wilson*.

(3) *Chris Perkins*.

(2) *Arles Taylor*.

(4)_____.

Date of Interview: *05 May 2005*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☒ Yes e)☐ No.
If Yes, brief description: *A proposed response amending the claims and providing arguments for the pending rejections*.

Claim(s) discussed: *1, 10, 13, 27, specifically, all in general*.

Identification of prior art discussed: *none*.

Agreement with respect to the claims f)☐ was reached. g)☒ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *See Continuation Sheet*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

MICHAEL WILSON
PRIMARY EXAMINER

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

RD

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: All of the outstanding rejections were discussed in relation to the proposed amendments and arguments. The amendment/arguments addressed all of the new matter rejections, except the phrase "wherein into said deleted U3 region..." and "after infection of target cell..." in claims 1, 13, 33, 39, 45 and 50. The amendment deletes using capsules for therapy and thereby addresses the enablement rejection regarding "capsules". The argument regarding enablement of amino acids 42-58 having anti-tumor activity will be considered upon filing the amendment. The amendments/arguments regarding the 112/2nd were discussed and will be considered upon filing the amendment. The overall structure of the claims was discussed. In particular, the examiner pointed out that the method claims should have the steps clearly set forth; the phrase "such that recombinant retroviral particles... are produced" is a function of the producer cells, not the retroviral vector as written. The phrase "after infection of a target cells by said recombinant retroviral particle" is a functional limitation either describing the retroviral particle, the 5' LTR or the 3' LTR, not the retroviral vector or producer cell as written.

JENKINS, WILSON & TAYLOR, P.A.

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DATE: April 29, 2005

TO: Examiner Michael C. Wilson

FAX NO.: (571) 273-0738

FROM: Chris Perkins

RE: Draft Amendment for 09/058,546

NUMBER OF PAGES TO FOLLOW: 30

If transmission is poor, or if you do not receive all pages, please call (919) 493-8000 as soon as possible.

COMMENTS: Examiner Wilson:

Please find attached a draft Amendment for your consideration ahead of the Telephone Interview we have re-scheduled for Thursday, May 5, 2005, at 2 pm. Arles Taylor and I will call you at your office telephone number, unless you would like us to call at a different number.

Thank you again for your understanding in re-scheduling the interview, and we look forward to discussing this application with you next week.

Best regards,
Chris Perkins

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Gunzburg *et al.*

Group Art Unit: 1632

Serial No.: 09/058,546

Examiner: Wilson, Michael C.

Filed: April 10, 1998

Docket No.: 1406-203 (previously 2316.1008-000)

Confirmation No.: 7592

For: RETROVIRAL VECTORS CARRYING SENESCENT CELL DERIVED INHIBITORS 1 (SDI-1) OR ANTISENSE SDI-1 NUCLEOTIDE SEQUENCES

* *

AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is responsive to the Official Action dated December 1, 2004, having a period for Response that expired on March 1, 2005. A three-month extension of the period for Response up to and including June 1, 2005 is hereby requested. Please charge the small entity extension fee of $510.00 to Deposit Account No. **50-0426**. Favorable reconsideration is respectfully requested in view of the following Amendments and Remarks.

AMENDMENTS

Please amend the subject application as follows:

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IN THE CLAIMS:

1. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence encoding an SDI-1 polypeptide or a functional fragment thereof, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) an SDI-1 coding sequence encoding said SDI-1 polypeptide or functional fragment thereof, wherein said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted, such that recombinant retroviral particles encoding an SDI-1 polypeptide or a functional fragment thereof are produced,

wherein

~~(i) said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation;~~

~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

2. (Previously presented) The method of Claim 1 wherein the retroviral vector comprises a DNA sequence encoding SDI-1.

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3. (Previously presented) The method of Claim 1, wherein the functional fragment comprises amino acids 1 to 71 of human SDI-1.

4. (Previously presented) The method of Claim 1, wherein the functional fragment comprises amino acids 42 to 58 of human SDI-1.

5-8. (Canceled)

9. (Previously presented) The method of Claim 2, wherein the DNA sequence encoding an SDI-1 polypeptide or a functional fragment thereof is under transcriptional control of a regulatory element selected from the group consisting of a target cell specific regulatory element, a target cell specific promoter, and an X-ray inducible promoter.

10. (Previously presented) The method of Claim 9 wherein the regulatory element is selected from the group consisting of a Whey Acidic Protein (WAP) regulatory element and a mouse mammary tumor virus (MMTV) regulatory element.

11. (Previously presented) The method of Claim 10 wherein the retroviral vector is pLXS-SDI1.

12. (Canceled)

13. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector encoding an SDI-1 polypeptide or a functional fragment thereof, the retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) a sequence encoding an SDI-1 polypeptide or a functional fragment thereof wherein said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted,

wherein

~~(i) said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation;~~

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~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

14. (Currently amended) The isolated producer cell line of Claim 13, wherein the isolated producer cell[[s]] line is a human cell line.

15-18. (Canceled)

19. (Previously presented) A pharmaceutical composition comprising the isolated producer cell line of Claim 13 and a pharmaceutically acceptable carrier or diluent.

20-25. (Canceled)

26. (Currently amended) A method for introducing a DNA sequence encoding an SDI-1 polypeptide or a functional fragment thereof[[,]] into a human cell *in vitro*, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of Claim 13.

27. (Currently amended) A method for treating a subject having a tumor or restenosis, the method comprising administering into the tumor or the site of restenosis of said subject ~~to the subject~~ a therapeutically effective amount of a recombinant retroviral particle produced by the isolated producer cell line of Claim 13 ~~at a site of the tumor or restenosis~~.

28-30. (Canceled)

31. (Currently amended) The method according to Claim 27 wherein the administering is by injection of the recombinant retroviral particle into the tumor or the site of restenosis of said subject ~~at a site of the tumor or restenosis~~.

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32. (Canceled)

33. (Currently amended) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence encoding an SDI-1 polypeptide, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) a coding sequence encoding the SDI-1 polypeptide, wherein said SDI-1 polypeptide inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted, such that recombinant retroviral particles encoding an SDI-1 polypeptide or a functional fragment thereof are produced,

wherein

~~(i) said SDI-1 polypeptide inhibits cell proliferation;~~

~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

34-35. (Canceled)

36. (Previously presented) The method of Claim 33 wherein the regulatory element or promoter is selected from the group consisting of a target cell specific regulatory element, a target cell specific promoter, and an X-ray inducible promoter.

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37. (Previously presented) The method of Claim 36 wherein the regulatory element is selected from the group consisting of a Whey Acidic Protein (WAP) regulatory element and a mouse mammary tumor virus (MMTV) regulatory element.

38. (Previously presented) The method of Claim 37 wherein the retroviral vector is pLXS-SDI1.

39. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector encoding an SDI-1 polypeptide, said retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) a sequence encoding an SDI-1 polypeptide, wherein said SDI-1 polypeptide inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted,

wherein

~~(i) said SDI-1 polypeptide inhibits cell proliferation;~~

~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

40. (Previously presented) The isolated producer cell line of Claim 39, wherein the isolated producer cell line is a human cell line.

41-42. (Canceled)

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43. (Previously presented) A method for introducing a DNA sequence encoding an SDI-1 polypeptide into a human cell *in vitro*, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of Claim 39.

44. (Previously presented) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence encoding a polypeptide comprising amino acids 1 to 71 of human SDI-1, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising a DNA sequence which encodes the polypeptide, wherein:

(i) the polypeptide inhibits cell proliferation; and

(ii) said producer cell comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

45. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector encoding a polypeptide comprising amino acids 1-71 of human SDI-1, said retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) a sequence encoding a polypeptide comprising amino acids 1-71 of human SDI-1, wherein said polypeptide comprising amino acids 1-71 of human SDI-1 inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted,

wherein

~~(i) said polypeptide inhibits cell proliferation;~~

~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or

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promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

46-47. (Canceled)

48. (Previously presented) A method for introducing a DNA sequence encoding a polypeptide comprising amino acids 1-71 of human SDI-1 into a human cell *in vitro*, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of Claim 45.

49. (Previously presented) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence encoding a polypeptide comprising amino acids 42 to 58 of human SDI-1, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising a DNA sequence which encodes the polypeptide, wherein:

(i) the polypeptide inhibits cell proliferation; and

(ii) said producer cell comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

50. (Currently amended) An isolated producer cell line stably transfected with a retroviral vector encoding a polypeptide comprising amino acids 42-58 of human SDI-1, said retroviral vector comprising in 5' to 3' order:

(a) a 5' LTR ~~region of the structure U3-R-U5~~;

(b) a sequence encoding a polypeptide comprising amino acids 42-58 of human SDI-1, wherein said polypeptide comprising amino acids 42-58 of human SDI-1 inhibits cell proliferation; and

(c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein ~~into said~~ sequences deleted from the U3 region ~~has been cloned~~ are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted,

wherein

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~~(i) said polypeptide inhibits cell proliferation;~~

~~(ii)~~ (i) after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said ~~completely or partially deleted U3 region~~ polylinker sequence and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell; and

~~(iii)~~ (ii) said isolated producer cell line comprises at least one DNA construct encoding a protein required for said retroviral vector to be packaged.

51-52. (Canceled)

53. (Previously presented) A method for introducing a DNA sequence encoding a polypeptide comprising amino acids 42-58 of human SDI-1 into a human cell *in vitro*, the method comprising infecting the human cell with a retroviral particle produced by the isolated producer cell line of Claim 50.

54. (Previously presented) A recombinant retroviral particle produced by the method of Claim 1.

55. (Previously presented) A pharmaceutical composition comprising the retroviral particle of Claim 54 and a pharmaceutically acceptable carrier or diluent.

56-64. (Canceled)

Please add the following new claims:

65. (New) A method for producing a recombinant retroviral particle, said particle comprising an RNA sequence encoding an SDI-1 polypeptide or a functional fragment thereof, the method comprising stably transfecting an isolated producer cell line with a retroviral vector comprising (a) a 5' LTR; (b) an SDI-1 coding sequence encoding said SDI-1 polypeptide or functional fragment thereof, wherein said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation; and (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein sequences

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deleted from the U3 region are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted, such that recombinant retroviral particles encoding an SDI-1 polypeptide or a functional fragment thereof are produced.

66. (New) An isolated producer cell line stably transfected with a retroviral vector encoding an SDI-1 polypeptide or a functional fragment thereof the retroviral vector comprising (a) a 5' LTR; (b) a sequence encoding an SDI-1 polypeptide or a functional fragment thereof wherein said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation; and (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein sequences deleted from the U3 region are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted.

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REMARKS

I. Status Summary

Claims 1-4, 9-11, 13-16, 19-21, 23, 26, 27, 313, 33, 36-55, 58, 59, 61, and 63 are pending in the present application and have been examined.

Claim 1 has been objected to upon the contention that the preamble does not correlate with the rest of the claim and because it includes extraneous information. Claims 1, 13, 14, 21, 27, 31, 59, and 63 have also been objected to on other formal grounds relating to certain phrases appearing in the claims.

Claims 1-4, 9-11, 13-16, 19-21, 23, 26, 27, 31, 33, 36-55, 58, 59, 61, and 63 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification does not describe the subject matter in such a way as to reasonably convey to the skilled artisan that the inventors had possession of the invention at the time the application was filed.

Claims 15, 16, 20, 21, 23, 27, 31, 32, 41, 42, 46, 47, 51, 52, 56-59, 61, and 63 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification, while being enabled for a method of treating restenosis or cancer by contacting the site of restenosis or cancer with a retrovirus encoding SDI-1 resulting in a therapeutic effect, does not reasonably provide enablement for using any mode of delivery as broadly claimed, using producer cells or capsules to treat disease, or using analogues or fragments of SDI-1 to treat disease.

Claims 13-16, 19-21, 23, 26, 27, 31, 32, 39-43, 45-48, 50-53, 59, 61, and 63 have been rejected under 35 U.S.C. § 112, second paragraph, upon several contentions that the claims are indefinite.

Claims 15, 16, 20, 21, 23, 41, 42, 46, 47, 51, 52, 58, 59, 61, and 63 have been canceled without prejudice. Applicants hereby reserve the right to file one or more continuation applications directed to the subject matter of the canceled claims.

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Previously withdrawn claims 5-7, 12, 18, 24, 25, 29, and 30 have been canceled without prejudice. Applicants hereby reserve the right to file one or more divisional applications directed to the subject matter of the canceled claims.

Claims 1, 13, 14, 26, 27, 31, 33, 39, 45, and 50 have been amended. Applicants respectfully submit that support for the amendments can be found throughout the specification as filed, including *inter alia* in the claims as filed. Additional support can be found on page 10, line 25, through page 11, line 7 (describing replacing the viral gag, pol, and/or env genes with "therapeutic genes or marker genes"), and in Example 3 (discussing the cloning of pLXS-SDI1). Additional support can be found in Figure 7 (map of pLXS-SDI1) (showing the SDI-1 sequences between the LTRs), on page 13, lines 1-25 (retrovirus structure and life cycle, describing promoter conversion), page 7, lines 18-22 (treatment of cancer and/or restenosis), page 8, lines 5-19 (administration nearby or at the site of a tumor), page 19, lines 5-6 (administration into sites such as an organ or to the site of a tumor), page 6, lines 20-21 (WAP and MMTV regulatory elements), on page 13, lines 19-21 (WAP regulatory elements), on page 14, lines 1-9 (regulatory elements from WAP, MMTV, and others), on page 14, line 16, through page 15, line 6 (WAP and MMTV regulatory elements), and page 8, line 22, through page 9, line 12 (functional SDI-1 fragments). Thus, no new matter has been added through the amendments to the claims.

New claims 65 and 66 have been added. Applicants respectfully submit that support for the amendments can be found throughout the specification as filed, including *inter alia* in the claims as filed. Additional support can be found on page 5, lines 19-21 (replication defective retroviral vector carrying a DNA sequence encoding SDI-1, a functional analogue, or a fragment thereof, which when introduced into a packing cell line would produce a retroviral particle comprising an RNA sequence encoding SDI-1, a functional analogue, or a fragment thereof), page 7, lines 6-9 (recombinant retroviral particle produced by culturing packaging cell lines comprising the disclosed retroviral vectors), page 6, lines 8-15 (retroviral vector comprises 5' LTR, coding sequences for SDI-1 or a fragment thereof, and a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence

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containing a regulator element or promoter), and page 6, lines 24-27 (packaging cell line comprising the disclosed retroviral vector and at least one DNA construct encoding proteins required for said retroviral vector to be packaged, which is a producer cell line).

Reconsideration of the application as amended and based on the remarks set forth herein below is respectfully requested.

II. Responses to the Objections to the Claims

Claims 1, 13, 14, 21, 27, 31, 59, and 63 have been objected to on several formal bases related to the claim language. According to the United States Patent and Trademark Office (hereinafter "the Patent Office"), the preamble of claim 1 does not correlate with the rest of the claim, and claim 1 includes extraneous information. The Patent Office further asserts that:

- the phrase "encoding an SDI-1 polypeptide or a functional fragment thereof" in claims 1, 13, *et al.*, should parallel the description of the retroviral vector in item b, which currently only requires an SDI-1 coding sequence;
- the phrase "said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation" in claims 1, 13, *et al.*, should be with the description of the sequence encoding an SDI-1 polypeptide or a functional fragment thereof in (b);
- the phrase "isolated producer cells line" in claim 14, line 2, is in improper tense
- the preamble of claim 21 uses awkward syntax and should be amended to recite "treating an individual having a tumor or restenosis"
- claims 21, 27, 31, 59, and 63 should be amended to recite "a method of treating a patient having a tumor or restenosis comprising administering a retroviral particle into the tumor or the site of restenosis of said patient"

After careful consideration of the objections, applicants respectfully traverse the rejections and submit the following remarks.

In each case, it appears that the Patent Office has identified language that it prefers for the phrases at issue. While applicants do not necessarily disagree that

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alternative language can be employed for the phrases at issue, applicants respectfully submit that the language of the claims clearly recites the subject matter of the claims. Thus, applicants respectfully submit that the instant objections are improper.

However, in an effort to facilitate the prosecution of the claims, applicants have amended the claims as follows.

Claims 1 and 33 have been amended to recite a method for producing a recombinant retroviral particle comprising an RNA sequence encoding an SDI-1 polypeptide or a functional fragment thereof, the method comprising stably transfecting an isolated producer cell line with a retroviral vector, said retroviral vector comprising in 5' to 3' order (a) a 5' LTR; (b) an SDI-1 coding sequence encoding said SDI-1 polypeptide or functional fragment thereof, wherein said SDI-1 polypeptide or functional fragment thereof inhibits cell proliferation; and (c) a 3' LTR region comprising a completely or partially deleted U3 region, wherein sequences deleted from the U3 region are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted, such that recombinant retroviral particles encoding an SDI-1 polypeptide or a functional fragment thereof are produced. Similar amendments have also been made to claims 13, 39, 45, and 50.

Applicants respectfully submit that the amendments to claims 1, 13, 33, 39, 45, and 50 address the first two objections listed above, namely the objections to the preambles of the claims and to the placement in the claims of the phrase "said SDI-1 polypeptide or a functional fragment thereof inhibits cell proliferation". Applicants respectfully request that these objections be withdrawn at this time.

Turning now to the objection to claim 14, line 2, the claim has been amended to recite "isolated producer cell line", which applicants respectfully submit addresses the instant objection.

The Patent Office next objects to the preamble of claim 21, which the Patent Office asserts uses awkward syntax. While applicants do not necessarily agree with the Patent Office concerning this objection, claim 21 has been canceled. Thus, the instant objection is believed to have been rendered moot.

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Claims 21, 27, 31, 59, and 63 have been objected to on the assertion that the phrase "administering to the individual at a site of the tumor or the restenosis the capsule of claim 15" (for example) can be written more clearly to describe the method of administration. Initially, applicants respectfully submit that claims 21, 59, and 63 have been canceled, and thus the objections as to these claims are believed to have been rendered moot. With regard to claims 27 and 31, applicants respectfully submit that they have amended claims 27 and 31 to recite a method for treating a subject having a tumor or restenosis, the method comprising administering into the tumor or the site of restenosis of said subject a therapeutically effective amount of a recombinant retroviral particle produced by the isolated producer cell line of Claim 13 (claim 27) and a method wherein the administering is by injection of the recombinant retroviral particle into the tumor or the site of restenosis of said subject (claim 31). Applicants respectfully submit that the instant amendments address the objections, and respectfully request that the objections be withdrawn at this time.

Finally, claim 63 has been objected to upon the contention that the claim is missing the phrase "or restenosis" after line 2 and before "a capsule". Applicants respectfully submit that claim 63 has been canceled, and thus the objection as to this claim is believed to have been rendered moot.

Applicants respectfully submit that the amendments to claims 1, 13, 33, 39, 45, and 50 are for the purposes of clarity only, and are not to be interpreted as a surrender of any subject matter encompassed by these claims prior to the instant amendments. Applicants further respectfully submit that the amendments to claims 1, 13, 33, 39, 45, and 50 in conjunction with the cancellation of claims 21, 59, and 63 address all of the objections to the claims, and thus respectfully request that the withdrawal of the objections and the allowance of claims 1, 13, 33, 39, 45, and 50 at this time.

III. Responses to the Rejections under 35 U.S.C. § 112, First Paragraph

III.A. Response to the Written Description Rejections

Claims 1-4, 9-11, 13-16, 19-21, 23, 26, 27, 31, 33, 36-55, 58, 59, 61, and 63 have been rejected under the written description requirement of 35 U.S.C. § 112, first

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paragraph, upon the contention that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors had possession of the invention at the time the application was filed. According to the Patent Office, the following phrases constitute new matter:

1. "in 5' to 3' order";
2. "wherein into said deleted U3 region has been cloned a polylinker sequence into which a regulatory element or a promoter has been inserted";
3. "after infection of a target cell... ...SDI-1 coding sequence in said target cell";
4. "at a site of the tumor or restenosis"; and
5. "Whey Acidic protein... ...regulatory elements".

The first three aspects of the instant rejection have been applied to claims 1, 13, 33, 39, 45, and 50, the fourth aspect has been applied to claims 21, 31, 59, and 63, and the last aspect has been applied to claim 37.

After careful consideration of the rejection and the Patent Office's bases therefor, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully submit that explicit, word-for-word support for a claim amendment need not be found in the specification, and such amendments are considered proper when it is clear to one of ordinary skill in the art after consideration of the specification that the applicants had possession of the invention as of the application filing date. Applicants respectfully submit that the elements asserted to be new matter are clearly supported by the specification.

III.A.1. Response to the First New Matter Rejection

With respect to the element "in 5' to 3' order", applicants respectfully submit that one of ordinary skill in the art would recognize that retroviral vectors have three main components: a 5' LTR, a body into which coding sequences can be cloned, and a 3' LTR. Applicants respectfully submit that the phrase "in 5' to 3' order" simply refers to the fact that the SDI-1 coding sequences are present within the body of the vector and not within either LTR. Support for this amendment can be found throughout the

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specification as filed, including particularly at page 10, line 25, through page 11, line 7 (describing replacing the viral gag, pol, and/or env genes with "therapeutic genes or marker genes"), and in Example 3 (discussing the cloning of pLXS-SDI1). Additional support can be found in Figure 7 (map of pLXS-SDI1), which shows the SDI-1 sequences between the LTRs.

Additionally, applicants respectfully submit that the specification discloses ProCon vectors, which are non-self-inactivating vectors that are characterized by the ability to "promoter convert". Applicants respectfully submit that the ProCon strategy relates to cloning a heterologous promoter(s) and/or a regulatory element(s) into 3' U3 deletions in retroviral vectors, which upon infection of a target cell "promoter convert" in order to express genes present within the body of the vector under the control of the heterologous promoter(s) and/or regulatory element(s). See, among other places, page 13, lines 1-25 (retrovirus structure and life cycle, describing promoter conversion). Thus, applicants respectfully submit that the ProCon strategy supports the presence of the SDI-1 coding sequences between the LTRs (*i.e.* in the body of the vector).

Accordingly, applicants respectfully submit that the phrase "in 5' to 3' order" is not new matter, and respectfully request the withdrawal of the first aspect of the instant rejection.

III.A.2. Response to the Second New Matter Rejection

Turning now to the second aspect of the instant rejection, the Patent Office asserts that the phrase "wherein into said deleted U3 region has been cloned a polylinker sequence into which a regulatory element or a promoter has been inserted" is not supported by the specification. Applicants respectfully direct the Patent Office's attention to claim 8 as originally filed. Original claim 8 recites "a retroviral vector... [comprising]... a 3' LTR region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence containing a regulatory element or a promoter...". Applicants respectfully submit that since the original claims are part of the disclosure, this claim supports the language of the amendment, namely that a polylinker containing a regulatory element or promoter is

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cloned into the region of the 3' LTR corresponding to the sequences deleted from the U3 region. Applicants further respectfully submit that when the disclosure is viewed in its entirety, it is clear that an embodiment of the presently disclosed subject matter is a ProCon retroviral vector, and ProCon vectors are produced by deleting some or all of the 3' U3 region and inserting a heterologous promoter into this deletion. See, among other places, page 13, lines 1-25 (retrovirus structure and life cycle, describing promoter conversion). In some embodiments, a polylinker sequence is first inserted into the deletion to facilitate cloning of the regulatory element(s) and/or promoter.

Accordingly, applicants respectfully submit that the second aspect of the instant rejection has been addressed, and respectfully request that it be withdrawn at this time.

III.A.3. Response to the Third New Matter Rejection

The Patent Office next asserts that the following phrase is new matter:

> after infection of a target cell by said recombinant retroviral particle, said U3 of said 5' long terminal repeat region is replaced by said completely or partially deleted U3 region and said regulatory element or promoter, resulting in said SDI-1 coding sequence becoming operatively linked to said regulatory element or promoter and said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell

Applicants respectfully submit that the phrase at issue is inherently supported by the specification in view of the mode of operation of retroviral vectors generally, and ProCon vectors in particular. See, among other places, page 13, lines 1-25 (retrovirus structure and life cycle, describing promoter conversion).

Applicants respectfully submit that the phrase at issue describes a phase of post-infection retroviral replication, as described on page 13 of the present U.S. patent application as filed among other places. Retroviral particles contain single plus-strand RNA genomes of the structure [5'-R-U5] – body – [3'-U3-R]. The DNA form of the retrovirus after infection (*i.e.* the form that results from reverse transcription and when integrated into a host genome is referred to as the provirus), however, has the structure [5'-U3-R-U5] – body – [3'-U3-R-U5]. The "completion" of the 5' and 3' LTRs after

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infection results from the reverse transcription reaction, which involves duplicating the sequence of the 3' U3 at the 5' end of the 5' LTR, and the duplication of the 5' U5 at the 3' end of the 3' LTR.

Applicants respectfully submit that this is what is being described by the phrase at issue. During promoter conversion, the 3' U3 region, which now contains a polylinker into which one or more regulatory elements and/or promoters have been cloned, becomes duplicated upstream of the body of the vector, which contains the SDI-1 coding sequences. The placement of the regulatory element(s) and/or promoter(s) upstream of the body of the vector results in any coding sequences present in the body of the vector (*e.g.* SDI-1 coding sequences) becoming operatively linked to the regulatory element(s) and/or promoter(s), which applicants respectfully submit results in "said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell" as recited in the phrase at issue. This process is also disclosed in the specification as filed, including particularly on page 13, lines 1-25.

Accordingly, applicants respectfully submit that when the specification of the instant application is viewed with reference to the knowledge of the skilled artisan, it is clear that the phrase at issue is supported by the specification. Thus, applicants respectfully request that the third aspect of the instant rejection be withdrawn, and the claims allowed at this time.

Summarily, applicants respectfully submit that the third aspect of the new matter rejection of claims 1, 13, 33, 39, 45, and 50 has been addressed.

III.A.4. Response to the Fourth New Matter Rejection

The Patent Office asserts that the phrase "at a site of the tumor or restenosis" in claims 21, 31, 59, and 63 is new matter. Applicants respectfully submit, however, that it is well known in the art that retroviral particles encoding therapeutic polypeptides can be introduced at sites where the activity of the encoded therapeutic polypeptides is desirable. Thus, applicants respectfully submit that the skilled artisan would understand that one of the possible strategies for using the claimed compositions would be to administer them to the subject "at a site of the tumor or restenosis".

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Applicants respectfully submit that the specification as filed further supports the phrase at issue. Applicants respectfully direct the Patent Office's attention to the following passages in the specification:

- the use of retroviral particles as above for the preparation of a medicament for the treatment of disorders and diseases responsive to the anti-proliferative activity of SDI-1; the use as above for the preparation of a medicament for the treatment of a cancer, or restenosis (*see* page 7, lines 18-22);
- a method [for the treatment of a disorder or disease responsive to the anti-proliferative activity of SDI-1] wherein the recombinant retroviral particle is administered as an injection... into the living animal body, including a human, nearby or at the site of the tumor (*see* page 8, lines 5-19); and
- recombinant retroviral particles may be administered to a wide variety of locations including, for example, into sites such as an organ or to the site of a tumor (*see* page 19, lines 5-6).

Furthermore, given the disclosure in the specification of methods and compositions for the treatment of cancer (*e.g.* a tumor) and restenosis, which can be administered "into sites such as an organ or to the site of a tumor", applicants respectfully submit that the specification supports the phrase "at a site of the tumor or restenosis" as it appears in amended claim 31 ("The method according to Claim 27 wherein the administering is by injection of the recombinant retroviral particle into the tumor or the site of restenosis of said subject").

Summarily, applicants respectfully submit that the phrase "at a site of the tumor or restenosis" appearing in claims 21, 31, 59, and 63 is fully supported by the specification as filed in conjunction with the knowledge of the skilled artisan. Claims 21, 59, and 63 have been canceled, and thus the rejection as to these claims is believed to have been rendered moot. Applicants respectfully submit, however, that the cancellation of claims 21, 59, and 63 is not to be viewed as acquiescence to the Patent Office's new matter assertion, or that by canceling these claims applicants surrender any subject matter encompassed by the canceled claims. Applicants reserve the right

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to file one or more continuation application directed to the subject matter of the canceled claims.

Accordingly, applicants respectfully submit that the fourth aspect of the instant new matter rejection has been addressed, and further that claim 31 is now in condition for allowance. Applicants respectfully request that the rejection be withdrawn and the claims allowed at this time.

III.A.5. Response to the Fifth New Matter Rejection

The Patent Office asserts that the phrase "Whey Acidic Protein (WAP) regulatory element and a mouse mammary tumor virus (MMTV) regulatory element" in claim 37 is new matter. Applicants respectfully submit, however, that the specification as filed clearly supports the use of WAP and MMTV regulatory elements. The Patent Office's attention is directed to claim 10 as filed, which recites "a retroviral vector according to Claim 9 wherein the target cell specific regulatory element is selected from WAP and MMTV regulatory elements". Thus, applicants respectfully submit that original claim 10 explicitly supports the phrase at issue. Additional support for this phrase can be found on page 6, lines 20-21 (WAP and MMTV), on page 13, lines 19-21 (WAP), on page 14, lines 1-9 (WAP, MMTV, and others), on page 14, line 16, through page 15, line 6 (WAP and MMTV).

Accordingly, applicants respectfully submit that the phrase at issue appearing in claim 37 is fully supported by the specification, and respectfully request that the fifth new matter rejection be withdrawn at this time. Applicants respectfully solicit a Notice of Allowance to that effect.

III.B. Responses to the Enablement Rejections

Claims 15, 16, 20, 21, 23, 27, 31, 32, 41, 42, 46, 47, 51, 52, 56-59, 61, and 63 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the specification, while being enabled for a method of treating restenosis or cancer by contacting the site of restenosis or cancer with a retrovirus encoding SDI-1 resulting in a therapeutic effect, does not reasonably provide enablement for using any mode of

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delivery as broadly claimed, using producer cells or capsules to treat disease, or using analogues or fragments of SDI-1 to treat disease. The Patent Office also asserts that the use of amino acids 42-58 of SDI-1 is not enabled.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully submit that claims 15, 16, 20, 21, 23, 32, 41, 42, 46, 47, 51, 52, 56-59, 61, and 63 have been canceled in this or a previous amendment. Thus, applicants respectfully submit that the instant rejection as been rendered moot as to these claims. The cancellation of these claims is strictly for the purpose of facilitating the prosecution of claims 27 and 31, and is not to be interpreted as a surrender of any subject matter encompassed by the canceled claims. Applicants reserve the right to file one or more continuation patent applications directed to the subject matter of the canceled claims.

Despite the cancellation of these claims, applicants wish to address certain assertions by the Patent Office with regard to the use of capsules *in vivo*. On page 9 of the Official Action, the Patent Office contends that the instant application does not contemplate using capsules containing producer cells or retroviral particles *in vivo*. Although the relevant claims have been canceled, applicants respectfully traverse this assertion. Applicants respectfully direct the Patent Office's attention to original claim 32, which recites a method for the treatment or a disorder or disease responsive to the anti-proliferative activity of SDI-1 by implanting into the living animal body, including a human, nearby or at the site of the tumor, an encapsulated packaging cell line comprising encapsulated cells having a core containing packaging cells. Similar disclosure is also provided on page 8, lines 16-19, and on page 19, line 17, through page 21, line 7, particularly at page 21, lines 4-7, which state "after a suitable period in culture... the cell containing capsules can be surgically implanted either directly, or by injection using a syringe into various areas of the body including the breast". Thus, applicants respectfully submit that the specification clearly supports *in vivo* use of capsules containing retrovirus or retrovirus producer cells.

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Turning now to the instant rejection as applied to pending claims 27 and 31, applicants respectfully submit that claim 27 has been amended to recite "A method for treating a subject having a tumor or restenosis, the method comprising administering into the tumor or the site of restenosis of said subject a therapeutically effective amount of a recombinant retroviral particle produced by the isolated producer cell line of Claim 13". Claim 31 has been similarly amended. Applicants respectfully submit that these claims now recite subject matter that the Patent Office concedes on page 6 of the Official Action is enabled. Thus, applicants respectfully request that the instant rejection of claims 27 and 31 be withdrawn at this time.

Turning now to the second aspect of the instant rejection regarding the use of amino acids 42-58 of SDI-1, the Patent Office asserts that the specification and the art at the time of filing did not teach that amino acids 42-58 of SDI-1 had the same function as full length SDI-1 or had any inhibitory effect *in vivo* (Official Action at pages 9-10). This element appears in currently pending claims 4, 49, 50, and 53.

Applicants respectfully direct the Patent Office's attention to the discussion beginning on page 8, line 22, of the specification. As disclosed therein,

> [T]he active domains of SDI-1 are present within amino acids 1-71. Active domains also comprise amino acids 42 to 47, 53 to 58 and 66 to 71. Deletion of amino acids 53 to 58 was found to result in the greatest loss of DNA synthesis inhibitory activity (50% of full length DNA). Deletion of amino acids 42 to 47 and 66 to 71 also resulted in a loss of inhibitory activity but to a much lesser extent. Deletion analysis have thus indicated that the critical region of SDI-1 polypeptide must lie between amino acids 42 to 71, and fine studies implicate that the region between amino acids 48 to 65 are critical for the negative growth effects of the gene.

Specification, pages 8-9. Thus, applicants respectfully submit that the specification discloses that amino acids 42-71 are involved in SDI-1 biological activity, and that the largest effect was seen when amino acids 53-58 were deleted. Applicants respectfully submit that the conclusion to be drawn from these data is that amino acids 42-58 contain a domain that has biological activity.

Thus, applicants respectfully submit that that one of ordinary skill in the art can easily confirm that this fragment contains inhibitory activity by referring to the guidance

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provided in the specification and by employing widely known molecular biology techniques. Applicants respectfully submit that the specification teaches the construction of ProCon SDI-1 retroviral vectors (*see e.g.* Example 3, beginning on page 23). Applicants further respectfully submit that the nucleic acid sequence encoding amino acids 42-58 is known, and can be amplified from plasmid PSDI1 (Noda *et al.*, also disclosed in Example 3) using PCR techniques that are known in the art (*see also* Example 3).

Thus, using the amplification product produced using the general strategy disclosed in Example 3 and depicted in Figure 7, one of ordinary skill in the art could create a ProCon retroviral vector encoding amino acids 42-58 without undue experimentation. This vector could then be employed in the strategies disclosed in Example 4 to test the ability of the resulting vector for anti-proliferative activity without undue experimentation. As a result, applicants respectfully submit that the specification enables the subject matter of claims 4, 49, 50, and 53 related to the fragment of SDI-1 containing amino acids 42-58, and thus respectfully request that the instant aspect of the enablement rejection be withdrawn at this time.

Accordingly, applicants respectfully submit that the rejections of pending claims 4, 27, 31, 49, 50, and 53 under the enablement requirement of 35 U.S.C. § 112, first paragraph, have been addressed, and that the claims are now in condition for allowance. Applicants respectfully solicit a Notice of Allowance to that effect.

IV. Claim Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 13-16, 19-21, 23, 26, 27, 31, 32, 39-43, 45-48, 50-53, 59, 61, and 63 have been rejected under 35 U.S.C. § 112, second paragraph, on several bases. After careful consideration of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

Initially, applicants respectfully submit that claims 15, 16, 20, 21, 23, 41, 42, 46, 47, 51, 52, 59, 61, and 63 have been canceled without prejudice, and thus the instant rejections are believed to have been rendered moot as to these claims. Thus,

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applicants respectfully submit that the following remarks are directed to the rejections as applied to the remaining pending claims.

There are several rejections under this section, which are summarized as follows:

No.	Claim(s)	Term or Phrase at Issue
1.	13, 39, 45, 50	"a 5' LTR region of the structure U3-R-U5"
2.	13, 39, 45, 50	"wherein into said deleted U3 region has been cloned a polylinker sequence into which a regulatory element or a promoter has been inserted"
3.	1	"after infection of a target cell... said SDI-1 coding sequence in said target cell"
4.	1	"replaced by said completely or partially deleted U3 region"
5.	13	"said recombinant retroviral particle"

IV.A. Response to the First 35 U.S.C. § 112, Second Paragraph, Rejection

Claims 13, 39, 45, and 50 have been rejected upon the assertion that the phrase "a 5' LTR region of the structure U3-R-U5 is unclear. According to the Patent Office, a 5' LTR having such a structure cannot be determined, because it cannot be determined how much of the U3, R, or U5 region is required to have the structure of a U3, R, or U5 region.

Applicants respectfully submit that the phrase at issue is intended to recite that the vector comprises a functional 5' LTR. As such, applicants respectfully submit that one of ordinary skill in the art would be able to determine when the metes and bounds of the relevant claims were met. Thus, applicants respectfully submit that the instant rejection is improper.

However, in an effort to facilitate the instant prosecution, claims 1, 13, 33, 39, 45, and 50 have been amended to remove the phrase at issue and recite "a 5' LTR". Applicants respectfully submit that the amendments to claims 1, 13, 33, 39, 45, and 50

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are for the purposes of clarity only, and are not to be interpreted as a surrender of any subject matter encompassed by these claims as originally filed.

Accordingly, applicants respectfully submit that the instant rejection under 35 U.S.C. § 112, second paragraph, has been addressed, and respectfully submit that the claims are in condition for allowance at this time.

IV. B. Response to the Second 112, Second Paragraph Rejection

Claims 13, 39, 45, and 50 have also been rejected upon the assertion that the phrase "wherein into said deleted U3 region has been cloned a polylinker sequence into which a regulatory element or a promoter has been inserted" is unclear. According to the Patent Office, the metes and bounds of this phrase are not clear because (a) the sequences encompassed by the phrase "polylinker sequence" cannot be determined; (b) it cannot be determined if the polylinkers have restrictions sites and a regulatory element/promoter or if the polylinkers are a regulatory element/promoter; (c) the phrase uses improper syntax; and (d) a polylinker inserted into a deleted U3 region would not be part of the retroviral vector because the polylinker would be part of a deleted region.

With regard to contention (a) applicants respectfully submit that the term "polylinker" is understood by the skilled artisan to refer to a stretch of nucleotides comprising one or more restrictions sites that facilitates the cloning of other nucleic acid molecules. This is consistent with the definition of "polylinker" that appears on page 16 of the specification, which states "the term 'polylinker' is used for a short stretch of artificially synthesized DNA which carriers a number of unique restriction sites allowing for the easy insertion of any promoter or DNA segment". Thus, applicants respectfully submit that one of ordinary skill in the art would understand that within the context used in the instant specification and claims, a polylinker is a stretch of nucleotides carrying unique restriction sites that are employed for cloning regulatory elements and/or promoters into retroviral vectors.

Furthermore, applicants respectfully submit that the specification thus clearly indicates that the polylinker is used as a location for cloning regulatory elements and/or promoters. Accordingly, applicants respectfully submit that that the Patent Office's

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second assertion listed hereinabove is an unsupported interpretation of the phrase at issue. Clearly, the polylinker allows insertion of regulatory elements and/or promoters, but itself is not necessarily a regulatory element or a promoter. Applicants respectfully submit that when the specification as a whole is considered in context, it is clear that the sequences that have been deleted from the 3' U3 region are replaced with a regulatory element and/or a promoter, and that a polylinker can be used to facilitate the cloning steps. Thus, applicants respectfully submit that the instant rejection is improper.

Nonetheless, in an effort to facilitate the instant prosecution, applicants have amended the phrase at issue in claims 1, 13, 33, 39, 45, and 50 to recite "wherein sequences deleted from the U3 region are replaced with a polylinker sequence into which a regulatory element or a promoter has been inserted". Support for this amendment is found in the subject U.S. patent application as filed at page 6, lines 10-12, among other places. Applicants respectfully submit that the amendments to these claims address the instant rejection. Applicants further respectfully submit that claims 1, 13, 33, 39, 45, and 50 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

IV.C. Response to the Third and Fourth
35 U.S.C. § 112, Second Paragraph, Rejections

Claims 1, 13, 39, 45, and 50 have been rejected upon the contention that the phrases "after infection of a target cell... said SDI-1 coding sequence in said target cell" and "replaced by said completely or partially deleted U3 region" render the claims indefinite. According to the Patent Office, it is unclear if the first phrase is describing a function of the retrovirus or a step in the method. The Patent Office also asserts that the deleted U3 region is gone and cannot replace anything.

Applicants respectfully submit that the phrase at issue describes a phase of post-infection retroviral replication, as described on page 13 of the present U.S. patent application as filed among other places. Retroviral particles contain single plus-strand RNA genomes of the structure [5'-R-U5] – body – [3'-U3-R]. The DNA form of the retrovirus after infection (*i.e.* the form that results from reverse transcription and when

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integrated into a host genome is referred to as the provirus), however, has the structure [5'-U3-R-U5] – body – [3'-U3-R-U5]. The "completion" of the 5' and 3' LTRs after infection results from the reverse transcription reaction, which involves duplicating the sequence of the 3' U3 at the 5' end of the 5' LTR, and the duplication of the 5' U5 at the 3' end of the 3' LTR.

Applicants respectfully submit that this is what is being described by the phrase at issue. During promoter conversion, the 3' U3 region, which now contains a polylinker into which one or more regulatory elements and/or promoters have been cloned, becomes duplicated upstream of the body of the vector, which contains the SDI-1 coding sequences. The placement of the regulatory element(s) and/or promoter(s) upstream of the body of the vector results in any coding sequences present in the body of the vector (*e.g.* SDI-1 coding sequences) becoming operatively linked to the regulatory element(s) and/or promoter(s), which applicants respectfully submit results in "said regulatory element or promoter regulating expression of said SDI-1 coding sequence in said target cell" as recited in the phrase at issue. Further the phrase at issue has been amended by deleting the phrase "completely or partially deleted U3 region" and inserting in place thereof the term "polylinker sequence". This process is also disclosed in the specification as filed, including particularly on page 13, lines 1-25.

Accordingly, applicants respectfully submit that when the specification of the instant application is viewed with reference to the knowledge of the skilled artisan, it is clear that the phrase at issue would be well understood. Thus, applicants respectfully request that the third and fourth aspect of the instant rejection be withdrawn, and the claims allowed at this time.

IV.D. Response to the Fifth 35 U.S.C. § 112, Second Paragraph, Rejection

Finally, the Patent Office asserts that the phrase "said recombinant retroviral particle" in claim 13 lacks antecedent basis. Applicants respectfully submit that that the phrase at issue has been removed from the claim. Thus, applicants respectfully submit that the instant rejection has been rendered moot, and respectfully request that it be withdrawn.

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Applicants further respectfully submit that that the rejections of claims 1, 13, 39, 45, and 50 under 35 U.S.C. § 112, second paragraph, have been addressed, and that the claims are now in condition for allowance. Applicants respectfully solicit a Notice of Allowance to that effect.

V. Discussion of New Claims

New claims 65 and 66 are added herein. Applicants respectfully submit that support for the amendments can be found throughout the specification as filed, including *inter alia* in the claims as filed. Additional support can be found on page 5, lines 19-21 (replication defective retroviral vector carrying a DNA sequence encoding SDI-1, a functional analogue, or a fragment thereof, which when introduced into a packing cell line would produce a retroviral particle comprising an RNA sequence encoding SDI-1, a functional analogue, or a fragment thereof), page 7, lines 6-9 (recombinant retroviral particle produced by culturing packaging cell lines comprising the disclosed retroviral vectors), page 6, lines 8-15 (retroviral vector comprises 5' LTR, coding sequences for SDI-1 or a fragment thereof, and a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence containing a regulator element or promoter), and page 6, lines 24-27 (packaging cell line comprising the disclosed retroviral vector and at least one DNA construct encoding proteins required for said retroviral vector to be packaged, which is a producer cell line).

New claims 65 and 66 are believed to be in condition for allowance based on the comments set forth herein above with respect to claims 1-4, 9-11, 13, 14, 19, 26, 27, 31, 33, 36-40, 43-45, 48-50, and 53-55. Allowance of new claims 65 and 66 is respectfully requested.

CONCLUSIONS

In light of the above amendments and remarks, applicants respectfully submit that claims 1-4, 9-11, 13, 14, 19, 26, 27, 31, 33, 36-40, 43-45, 48-50, 53-55, and 65-66 are in condition for allowance at this time, and respectfully solicit a Notice of Allowance to that effect.

FOR THE PURPOSES OF INTERVIEW ONLY:
DO NOT ENTER AMENDMENT

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,
JENKINS, WILSON & TAYLOR, P.A.

Date: **DRAFT – DRAFT – DRAFT** By: **DRAFT – DRAFT – DRAFT – DRAFT**

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